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Case Report

A CASE OF ADULT ONSET BARTTER'S SYNDROME

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ABSTRACT
Bartter's syndrome consists of genetically heterogeneous group of disorders presenting with features of salt losing tubulopathy of frusemide type which is characterised by polyuria, hypokalaemia, hypochloraemia, metabolic alkalosis, normal blood pressure with hyerreninemic hyperaldosteonism. We report a case of 25 year old male presenting with paraparesis and Bartter like phenotypic presentation. We report this case because of its presentation in adults which is rare.

Keywords: *Bartter's Syndrome, Diuretic Abuse, Hypokalaemia, Metabolic Alkalosis*

INTRODUCTION
Bartter's syndrome, a hereditary disorder linked to mutation in five genes (Lee *et al.,* 2012) with autosomal recessive (type1-4) or autosomal dominant pattern (type 5) mode of inheritance. These genetic defect affect ion transport channels in thick ascending loop of Henle and distal convoluted tubule. 30% of the filtered Na and Cl is reabsorbed in thick ascending limb, which when affected lead to defective reabsorption is the main pathology. The antenatal variants are type 1, 2 and 4 with defect in NKCC2, ROMK and BARTTIN, a ß subunit for CLCKa and CLCKb transport channels respectively. Type 3 (classical variant) present with early childhood or continue into adulthood[2], defect in CLCNKb channel and nephrocalcinosis is not a constant feature. Type 5 (hypocalcaemia with bartter) due to gain of function mutation in CaR channel, so it is associated with hypoparathyroidism (Yamamoto *et al.,* 2000) and hypomagnesimia (Waldegger, 2008). The main differentials to be excluded are Gitelman syndrome and pseudo Bartter (diuretic abuse and surreptitious vomiting, cystic fibrosis). The prevalence of Gitelman syndrome was 1 in 40,000 compared with 1 in 1,000,000 for Bartter syndrome (Ji *et al.,* 2008). The lower prevalence of Bartter syndrome in the population may be due at least in part to prenatal or neonatal death resulting from the disorder before it could be diagnosed. So, its presentation in adults is rare (Xiumin *et al.,* 2013; García Castaño *et al.,* 2013; Simon *et al.,* 1997).

CASES
A 25 year old male who is an alcoholic, smoker, presented with sudden onset weakness of both legs for 1 day. History of difficulty in using both upper and lower limbs. He has a history of strenuous exercise following which he developed this deficit.

Patient had a previous history of similar episode in past for which he took treatment and was not on regular follow up. Patient had no history of gastro intestinal loss. No history of drug intake like insulin, diuretic, antibiotics.

Patient was born to non-consanguineous parents. No history of similar episode among family members. On examination- BP-110/70 mmHg, PR-98/min, SPO2-90%, single breath count was 10. Neurological examination- power of both upper and lower limb were 1/5. Hand grip was 80%. Deep tendon reflexes were absent. Sensory, autonomic and cranial nerve examination were normal. No deafness or growth retardation.

Investigation revealed Serum potassium-1.7meq/L, serum sodium-146meq/L, random blood sugar-100mg/dl, arterial blood gas analysis showed pH-7.46, HCO_3-25.4 mmol/L, pCO_2- 37.3 mmHg, Na^+-146 mmol/L, K^+-2.84 mmol/L. Urine potassium was 24 mmol/day and Trans tubular gradient was 5.63 indicated increased distal potassium secretion. Urine chloride level was 111mmol/day, urine calcium/creatinine ratio was 0.311. Serum magnesium was 2.00mg/dl. Thyroid function test was normal. Hypokalemia, normal blood pressure, metabolic alkalosis, hypercalciuria, normal magnesium level lead to diagnosis of Bartter's syndrome.

DISCUSSION

In Bartter's syndrome, most common mutated gene is KCNJ1. Deafness points to BSND defect, neonatal history of hyperkalaemia later followed by hypokalaemia points to KCNJ1 defect, CLCNKB defect has severe metabolic alkalosis. The genetic defects affect the ion transport channels in thick ascending loop of Henle and distal convoluted tubule. Gitelman syndrome is differentiated from Bartters by its late presentation and it is thiazide like salt losing tubulopathy. Features like hypo magnesia, hypocalciuria and chrondrocalcinosis (Waldegger, 2008) occur only in Gitelman not in Bartter's syndrome.

The features of Bartter's include polyuria, polydipsia, and decreased concentrating ability (Kurtz, 1998; Stein, 1985). Chronic fatigue, muscle weakness, cramps, constipation and recurrent vomiting, paralysis. Growth retardation, hypokalaemic nephropathy and nephrocalcinosis are some long term effects.

Our patient presented with sudden onset weakness of lower limbs with preserved sensory and autonomic functions. He had no feature of polyuria or polydipsia.

Dysfunction of the channels described previously lead to hypokalemia, hypochloremia, hypercalciuria. Hypokalemia is due to compensatory mechanism that is activated to absorb more Nacl downstream. This also leads to metabolic alkalosis.

Hypomagnesemia occurs in 20% of cases (Walsh *et al.,* 2011). hypercalciuria and nephrocalcinosis occur in type 1,2 not in type 4, rare in type 3. Stimulation of renin-angiotensin axis and activation of TGF-ß is responsible for renal changes (Yamamoto *et al.,* 1996). Even with high angiotensin II they have low/normal blood pressure due to renal release of prostaglandin E2. Prostaglandin E2 production due to increased cyclooxygenase 2 (COX2) expression (Kömhoff *et al.,* 2004). So, these patients do not develop hypertension or its complications (Pagnin *et al.,* 2006).

Our patient presented with hypokalaemia, hypochloraemia, metabolic alkalosis, with hypercalciuria. Serum magnesium levels were normal. Nephrocalcinosis was absent. Patients' blood pressure was normal. Urine potassium was elevated. Transtubular potassium gradient (TTKG) was >4. Urine chloride and urine calcium creatinine ratio was elevated. USG and CT abdomen was normal.

Treatment includes oral potassium supplementation (1 to 3mmol/kg/day) mainly potassium chloride is preferred. NSAID (indomethacin 2 to 4 mg/kg/day) and high dose spironolactone (2 to 5 mg/kg) or amiloride (10to 15 mg/kg) can be given and magnesium salts can be given. Increasing oral salt intake is not acceptable as it leads to more potassium loss.

Our patient was treated with oral potassium chloride supplementation and patient recovered from weakness.

The prognosis of Bartter's syndrome depends on the type, among which type 3 and 5 appear to be less severe than type 1 and 2. In long term 25% develop mild impairment of kidney (Jeck *et al.,* 2001). Only few data's about long term follow up of adult patients with Bartter's syndrome is available. End stage renal disease is uncommon in Bartter's syndrome (Puricelli *et al.,* 2010).

REFERENCES

García Castaño A, Pérez de Nanclares G, Madariaga L *et al.*, (2013). Genetics of type III Bartter syndrome in Spain, proposed diagnostic algorithm. *PLoS One* **8** e74673.

Jeck N, Reinalter SC, Henne T *et al.*, (2001). Hypokalemic salt-losing tubulopathy with chronic renal failure and sensorineural deafness. *Pediatrics* **108** E5.

Ji W, Foo JN, O'Roak BJ *et al.*, (2008). Rare independent mutations in renal salt handling genes contribute to blood pressure variation. *Nature Genetics* **40** 592-599.

Kömhoff M, Reinalter SC, Gröne HJ and Seyberth HW (2004). Induction of microsomal prostaglandin E2 synthase in the macula densa in children with hypokalemic salt-losing tubulopathies. *Pediatric Research* **55** 261-6.

Kurtz I (1998). Molecular pathogenesis of Bartter's and Gitelman's syndromes. *Kidney International* **54** 1396-1410.

Lee BH, Cho HY, Lee H *et al.*, (2012). Genetic basis of Bartter syndrome in Korea. *Nephrology Dialysis Transplantation* **27** 1516-21.

Pagnin E, Davis PA, Semplicini A and Calò LA (2006). The search for a link between inflammation and hypertension: contribution from Bartter's/Gitelman's syndromes. *Nephrology Dialysis Transplantation* **21** 2340-2.
Puricelli E, Bettinelli A, Borsa N *et al.*, (2010). Long-term follow-up of patients with Bartter syndrome type I and II. *Nephrology Dialysis Transplantation* **25** 2976-81.
Simon DB, Bindra RS, Mansfield TA *et al.*, (1997). Mutations in the chloride channel gene, CLCNKB, cause Bartter's syndrome type III. *Nature Genetics* **17** 171-8.
Stein JH (1985). The pathogenetic spectrum of Bartter's syndrome. *Kidney International* **28** 85-93.
Waldegger S (2008). Bartter, Gitelman, and related syndromes. In: Geary DF, Schaefer F, edition, *Comprehensive Pediatric Nephrology,* (USA, Philadelphia: Mosby) 450-459
Walsh SB, Unwin E, Vargas-Poussou R, Houillier P and Unwin R (2011). Does hypokalaemia cause nephropathy? An observational study of renal function in patients with Bartter or Gitelman syndrome. *Quarterly Journal of Medicine* **104**(11) 939-44.
Xiumin W, Zheng S, Meichun X, Junfen F and Li L (2013). A Chinese girl with Bartter syndrome type III due to a novel mutation and/or single nucleotide polymorphisms (SNPs) in CLCNKB gene. *Iranian Journal of Pediatrics* **23** 89-94.
Yamamoto M, Akatsu T, Nagase T *et al.*, (2000). Comparison of hypocalcemic hypercalciuria between patients with idiopathic hypoparathyroidism and those with gain-of-function mutations in the calcium-sensing receptor: is it possible to differentiate the two disorders? *The Journal of Clinical Endocrinology & Metabolism* **85** 4583-4591.
Yamamoto T, Noble NA, Cohen AH *et al.*, (1996). Expression of transforming growth factor-beta isoforms in human glomerular diseases. *Kidney International* **49** 461-9.
Zelikovic I, Szargel R, Hawash A, Labay V, Hatib I, Cohen N and Nakhoul F (2003). A novel mutation in the chloride channel gene, CLCNKB, as a cause of Gitelman and Bartter syndromes. *Kidney International* **63** 24-32.